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July 12, 2002

Quinn Intellectual Property Law Group, P.C.

By:

Client's Attorney

JUL 19 2002

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty Docket No.: 407T-893910US

Client Ref: UC 99-279-2

In re application of:

PAUL A. PRICE

Application No.: 10/045,596

Filed: 10/18/2001

For: **A FETUIN-MGP-MINERAL
COMPLEX IN SERUM**

Examiner: unassigned

Art Unit: unassigned

**PRELIMINARY AMENDMENT TO
ACCOMPANY NOTICE OF MISSING
PARTS**

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This preliminary amendment accompanies the Notice to File Missing Parts of Nonprovisional Application mailed on April 24, 2002, containing instructions to comply with the requirements of 37 C.F.R. §§1.821-1.825. The following documents are enclosed herewith:

- 1) A petition to extend the period of response for one month;
- 2) An initial Computer readable form (CRF) copy of the Sequence Listing; and
- 3) An initial paper copy of the Sequence Listing.

Please amend the claims and/or specification as follows

IN THE SPECIFICATION.

After the abstract, please insert the accompanying sequence listing (page1).

Delete paragraph 176 on page 62 and insert the following:

--[0001] We next examined the possible sedimentation of the serum calcium phosphate complex during centrifugation, a property that might be anticipated for the complex based on the fact that calcium phosphate mineral phases typically have densities about 3 fold greater than serum. As shown in Table II, centrifugation of serum from rats treated with the 32mg dose of etidronate resulted in a pellet containing calcium, phosphate, and MGP. When the pellet was dissolved in acid

and analyzed by SDS-PAGE, a major band was found at 59 kDa which accounted for at least 80% of the Coomassie staining (Figure **Error! Reference source not found.**). When this component was electrophoretically transferred to PVDF and subjected to N-terminal protein sequencing, one sequence was obtained, A-P-Q-G-A-G-L-G-F-R- (SEQ ID NO:1), which matches the N-terminal sequence of rat fetuin (Ohnishi *et al.* (1993)-*J. Bone and Mineral Res.* 8: 367-377). The other major band in the gel had an apparent molecular weight of 66 kDa and accounted for about 10% of the total Coomassie staining; this band was identified as rat serum albumin by N-terminal sequence analysis. Based on the recovery of fetuin in the pellet, we estimate the weight ratio of fetuin to mineral phosphate in the pellet to be 3.4 mg/mg. Since the supernatant level of calcium and phosphate remained above the level in control serum (Table II), it is likely that centrifugation did not sediment all of the calcium complex in these experiments.--

In accordance with 37 CFR §1.121 a marked up version of the above-amended paragraph(s) illustrating the changes introduced by the forgoing amendment(s) are provided in Appendix C.

REMARKS

This preliminary amendment is provided in Response to the Notice to File Missing Parts of Nonprovisional Application. Applicant(s) request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the sequences (SEQ ID NO:1) in computer readable form, and a paper copy of the sequence information that has been printed from the floppy disk.

The information contained in the computer readable form (floppy disk) was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy.

This amendment contains no new matter. The amendments to the specification and/or claims are to provide a formal sequence listing and/or to provide appropriate cross-references to SEQ ID Numbers in accordance with 37 C.F.R. §§1.821 to 1.825. The sequence information provided herein finds support in the specification as filed.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

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Respectfully submitted,



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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE IN 10/045,596 WITH ENTRY
OF THIS AMENDMENT

In the specification:

[0002] We next examined the possible sedimentation of the serum calcium phosphate complex during centrifugation, a property that might be anticipated for the complex based on the fact that calcium phosphate mineral phases typically have densities about 3 fold greater than serum. As shown in Table II, centrifugation of serum from rats treated with the 32mg dose of etidronate resulted in a pellet containing calcium, phosphate, and MGP. When the pellet was dissolved in acid and analyzed by SDS-PAGE, a major band was found at 59 kDa which accounted for at least 80% of the Coomassie staining (Figure **Error! Reference source not found.**). When this component was electrophoretically transferred to PVDF and subjected to N-terminal protein sequencing, one sequence was obtained, A-P-Q-G-A-G-L-G-F-R- (SEQ ID NO:[]1), which matches the N-terminal sequence of rat fetuin (Ohnishi *et al.* (1993) *J. Bone and Mineral Res.* 8: 367-377). The other major band in the gel had an apparent molecular weight of 66 kDa and accounted for about 10% of the total Coomassie staining; this band was identified as rat serum albumin by N-terminal sequence analysis. Based on the recovery of fetuin in the pellet, we estimate the weight ratio of fetuin to mineral phosphate in the pellet to be 3.4 mg/mg. Since the supernatant level of calcium and phosphate remained above the level in control serum (Table II), it is likely that centrifugation did not sediment all of the calcium complex in these experiments.